UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/624,328	07/22/2003	John McMichael	13024/38627A	6971

4743 7590 10/21/2009

MARSHALL, GERSTEIN & BORUN LLP
233 SOUTH WACKER DRIVE
6300 SEARS TOWER
CHICAGO, IL 60606-6357

EXAMINER	
HUGHES, ALICIA R	

ART UNIT	PAPER NUMBER
1614	

MAIL DATE	DELIVERY MODE
10/21/2009	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/624,328	MCMICHAEL ET AL.	
	Examiner	Art Unit	
	Alicia Hughes	1614	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *01/09/2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,2,4,5,8-18 and 20-24* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,2,4,5,8-18 and 20-24* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Status of the Claims

Claims 1, 2, 4, 5, 8-18, and 20-24 of the subject application are pending.

Very regrettably, consideration of the claims and the decision of the Board of Appeals and Interferences, decided 6/25/09, has revealed some inconsistencies that this Action is set forth in order to correct and clarify. In particular, the affirming of the rejection of claim 15 conflicts with claim 16 wherein symptoms of sleep disorders in a patient are effectively treated with nerve growth factor because in the affirmed 103(a) rejection citing Siuciak it is seen that Suiciak at column 6, lines 48-55, describes sleep disorder treatment in a relatively short list of treated disorders. Another inconsistency is that said Siuciak also teaches subcutaneous etc. administration modes at column 6, lines 1-8, which are embodiments of instant claim 10, not previously rejected in the affirmed 103(a) rejection. Additionally, the below Office action contains new prior art issues which have become known to the examiner. Normally, the procedure that would be appropriate would be as defined in MPEP 1214.06[R-3], section I, paragraph 12.119.01; however, in this case, the above inconsistencies support the setting forth of this action as more appropriate.

Again, very regrettably this action is a reopening of prosecution after the decision of the Board of Appeals and Interferences of 6/25/09 and any inconvenience to appellant is regretted.

Claim Rejections – 35 U.S.C. §103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

First 103(a) Rejection(essentially repeated as affirmed in the 6/25/09 decision of the Board of Appeals and Interferences)

Claims 1, 2, 4, 5, 9-16, and 20-24 are rejected under 35 U.S.C. 103(a) as being obvious over U.S. Patent No. 5,599,560 [hereinafter referred to as "Siuciak"] in view of the Merck Manual.

Siuciak discloses that it is known in the art that neurotrophic factors (Col. 6, lines 16-31) is used for the treatment of depression as well as panic disorders (Col. 6, lines 44-65) and sleep disorders (Col. 6, lines 48-55). Suiciak also disclose the administration of neurotrophic factors intravenously, subcutaneously and via oral mucosa (reasonably interpreted as inclusive of sublingual administration) (See column 6, lines 1-8.).

Importantly, Siuciak was already an issued patent on the date to which the Applicants claim priority. Siuciak teaches that "[t]he neurotrophin family ***includes*** brain-derived neurotrophic factor (BDNF), neurotrophin-3 (NT-3) and neurotrophin-4 (NT-4), all of which have recently been molecularly cloned and shown to be members of the nerve growth factor (NGF) family by virtue of their sequence homology" (Col. 2, lines 48-62)(emphasis added). The word "includes" implies that there are other members of the neurotrophin family in addition to the three listed, specifically. *See e.g. Mars Inc. v. H.J. Heinz Co.*, 377 F. 3d 1369, 1376 (Fed. Cir. 2004)(The word comprising is synonymous with the words including, containing, and characterized by, and all of these words are open-ended or inclusive and does not exclude additional, unrecited elements or agents).

Siuciak teaches that "[b]ased on the activity of neurotrophic factors, especially those members of the neurotrophin family ... applicants have discovered that the neurotrophins are useful for the treatment of depression" (Col. 4, lines 64-67).

The Merck Manual discloses that the definition of depression (a unipolar) disorder falls under a broad class of mood or affective disorders (Page 1525). The Merck Manual also states that individuals with mixed anxiety-depression possess conditions of symptoms that have both anxiety and depression (page 1529) and that depressed patients are anxious and depressed, typically (page 1531). The Merck Manual specifically discloses to the skilled artisan that a patient with the condition of PMS is characterized, *inter alia*, by anxiety and depression (page 1932).

Although Siuciak is silent to the use of NGF to treat the psychological conditions of PMS, anxiety disorders, and panic attacks, Siuciak does in fact teach and provide the artisan with the necessary motivation to use neurotrophic factors in the treatment of affective and anxiety disorders (Col. 6, lines 44-65).

Moreover, the determination of a specific range of a dosage having the optimum therapeutic index is well within the level of knowledge of one having ordinary skill in the art, and the artisan would be motivated to practice a reasonably wide range of dosages in order to determine optimum amounts to get the maximum effect of the drug while minimizing unwanted and/or adverse side effects as a matter of general practice. Hence, Siucuak in view of the Merck Manual make obvious the claimed subject matter.

Accordingly, one having ordinary skill in the art would have recognized that by treating depression and anxiety, one would also be treating and alleviating the symptoms of related

conditions and ailments that have depression and anxiety as symptoms, namely anxiety disorders, PMS, and depression associated with menustration and anxiety associated with panic attacks, most especially in view of the teaching of the Merck Manual.

In traversing the above rejection, Applicants argue that (1) nerve growth factor is a different protein than BDNF, NT-3 and NT-4, known to have different properties; (2) the Merck Manual do not overcome the deficiency in Siuciak, because Merck Manual neither teach nor suggest the use of NGF for the treatment of any disease, let alone for the treatment of psychological disorders disclosed in the contemplated invention; and (3) the only motivation or suggestion to combine Siuciak with the Merck Manual to alleviate the symptoms of psychological disorders arises from disclosures of the present invention and therefore, constitute impermissible hindsight. The above discussion explains the nerve growth factor family disclosure as being inclusive of BDNF etc. which responds to this argument, which therefore is non-persuasive.

To further bolster, rather than to establish the Applicants' position, it is noted that the Applicants' specification teaches that "[n]erve growth factor (NGF) [is] a prototypical neurotrophic factor and member of the neurotrophin family ... (Page 12, lines 27-28). Furthermore, "there remains a desire to use NGF to remedy other neurological disorders ... [such as] depression, anxiety, [and] bipolar disorder" (Specification p. 13, lines 19-23).

It is non-persuasive for the Applicants to argue that NGF illustrates the typical qualities of neurotrophic factors and members of the neurotrophin family and then to say that the teachings in Siuciak do not make the disclosure of the instant invention obvious, because it "does not teach the use of NGF which is a different protein for the treatment of depression and other

psychological disorders". If NGF is a prototypical neurotrophic factor and a member of the neurotrophin family claimed to treat depression, just as the neurotrophins in Siuciak, it would go without saying that the teachings of Siuciak make the present invention obvious, particularly in view of the Merck Manual disclosure, as discussed, *infra*.

The requisite motivation to combine references is present, because although Siuciak is silent as to the use of NGF to treat the psychological conditions of PMS and panic attacks, explicitly, the same does teach the use of NGF to treat affective disorders and anxiety disorders. The Merck Manual merely defines affective and anxiety disorders more clearly to include the alleviation of symptoms of related conditions and ailments that have depression and anxiety as symptoms, namely anxiety disorders, PMS and panic attacks.

In view of the foregoing, the rejection that claims 1, 2, 4, 5, 9-16, and 20-24 are *prima facie* obvious over Siuciak in view of the Merck Manual.

Second 103(a) Rejection

Claim 18 is rejected under 35 U.S.C. 103(a) as being obvious over U.S. Patent Pre-Grant Publication No. 2002/0002269 A1 [hereinafter referred to as "Milbrandt et al"].

Claim 18 is directed to a method of alleviating constipation comprising administering to a patient in need thereof, a therapeutically effective amount of nerve growth factor.

Milbrandt et al teach that nerve growth factor was the first neurotrophic factor identified and characterized (Page 1, Para. 007) and discloses a "new growth factor, artemin, which promotes cell survival and growth" (Page 2, Col. 2, Para. 15). Milbrandt et al goes further to explain that artemin compositions can be used to treat constipation (Page 12, Cols. 1-2, Paras. 112 and 113; Page 24, Col. 2, Claims 33 and 38).

In view of the foregoing, it would have been *prima facie* obvious to one of ordinary skill in the art at the time the instant invention was disclosed to use a nerve growth factor to treat constipation.

Third 103(a) Rejection

Claims 8, 9 and 17 are rejected under 35 U.S.C. 103(a) as being obvious over Siuciak in view of the Merck Manual and in further view of Steiner, M., "PMS versus PMDD: Diagnosis and Classification," *European Neuropsychopharmacology*, Vol. 9, Supplement 5, Page 145 (September 1999)[hereinafter referred to as "Steiner"] and O'Brien, P.M.S., "Somatic and Psychic Symptoms of PMD," *European Neuropsychopharmacology*, Vol. 9, Supplement 5, Page 145 (September 1999)[hereinafter referred to as "O'Brien"].

The teachings of the Merck Manual and of Siuciak, *supra*, are incorporated herein by reference in their entirety. However, neither reference explicitly teaches alleviating premenstrual dysphoric disorder ["PMDD"], or tension headaches by administering nerve growth factor. However, it is well-known in the pharmacological arts that tension, depression and anxiety are common symptoms of PMDD and PMS. See *e.g.*, Steiner at Para. 1. And further, headaches are a common symptom of PMS. See e.g., O'Brien at Para. 7.

It would be well within the purview of the skilled artisan to conclude that when one uses nerve growth factor to treat headaches, panic attacks, anxiety disorders, etc, he or she necessarily treats PMDD and PMS, too, most especially given their symptomatic interrelationship.

In view of the foregoing, and for all of the reasons made of record, it would have been prima facie obvious to one of ordinary skill in the art at the time the instant invention was contemplated to use nerve growth factor to treat PMS, PMDD and resultant tension headaches.

Conclusion

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Alicia Hughes whose telephone number is 571-272-6026. The examiner can normally be reached from 9:00 AM to 5:00 PM, Monday through Friday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ardin Marschel, can be reached at 571-272-0718. The fax number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR of Public PAIR. Status information for unpublished applications is available through Public PAIR only. For information about the PAIR system, see http://pair-direct-uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Alicia R. Hughes/
Examiner, Art Unit 1614

/Ardin Marschel/

Supervisory Patent Examiner, Art Unit 1614

/Remy Yucel/
Director, Technology Center 1600